REMARKS

I. Introduction

Receipt of a non-final Office Action dated August 30, 2005, is acknowledged. In the Action, the claims were rejected for obviousness-type double patenting over Wood *et al.*, U.S. Patent No. 6,264,922 ("Wood") (claims 28-40 and 42-45), and separately, over Saidi *et al.*, U.S. Patent No. 6,241,969 ("Saidi") (claims 28-40, 42-45 and 50-59).

Claims 28-40, 42-45, and 50-59 were also rejected as allegedly obvious over Liversidge *et al.*, U.S. Patent No. 5,145,684 ("Liversidge"), in view of Folke Moren, AEROSOLS IN MEDICINE, PRINCIPLES, DIAGNOSIS AND THERAPY, Chapter 13, pp. 321-350, Elsevier Science Publisher (1993) ("Moren"), or in view of A.R. Gennaro, REMINGTON'S PHARMACEUTICAL SCIENCES, 17TH ED., Chapter 93, pp. 1670-77 (1985) ("Gennaro") and Dieter Kohler, AEROSOLS IN MEDICINE, PRINCIPLES, DIAGNOSIS AND THERAPY, Chapter 12, pp. 303-19, (1993) ("Kohler").

Applicants respectfully request reconsideration of the present application in view of the reasons that follow.

II. Status of the Claims

Claims 28-40, 42-45, and 47-59 are pending and under examination. No amendments to the claims have been made.

III. Double Patenting Rejection

A. Wood Reference

The Office maintained the double patenting rejection over Wood, U.S. Patent No. 6,264,922, stating that a terminal disclaimer for Wood was not filed despite remarks to the contrary in a Response dated February 4, 2005. Applicants respectfully traverse this ground for rejection.

Submitted herewith is a copy of the Wood terminal disclaimer, as filed in February, and a copy of the stamped postcard from the PTO acknowledging receipt of the terminal

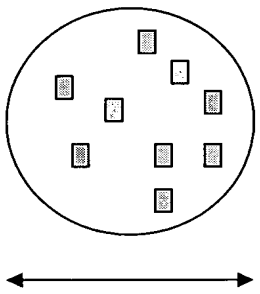
disclaimer. Accordingly, Applicants respectfully request the double patenting rejection over Wood be withdrawn.

B. Saidi Reference

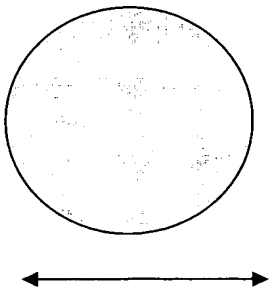
Claims 28-40, 42-45 and 51-59 were rejected under the judicially created doctrine of obviousness-type double patenting over claims 20-24 of Saidi *et al.*, U.S. Patent No. 6,241,969. In particular, the claims were rejected because "Saidi et al. is drawn to compositions containing corticosterioid compounds as active agents for the treatment of ailments and diseases of the respiratory tract, particularly the lungs through inhaled delivery with a nebulizer or for nasal delivery." Office Action at 5. Applicants respectfully traverse this ground for rejection.

Applicants believe that the examiner incorrectly levied a double patenting rejection. Saidi is assigned to Elan Corporation plc, which is distinct from Elan Pharma International Ltd. Therefore, the present application and the Saidi patent are not by the same inventive entity or commonly assigned.

Nevertheless, Saidi is not prior art. The Saidi patent describes compositions in which the corticosteroid is dissolved, and nebulizers with a droplet size in the range of 0.5 to 5 microns. *See e.g.*, Saidi at col. 9, lines 35-36. It is important, however, to differentiate between the liquid droplet size and the drug particle size. The present invention discloses that the droplet size is less than about 50 microns (50,000 nm) and the drug particle size is in the submicron range. The concept of drug particle size, however, is irrelevant in the Saidi patent because the drug is in solution. *See* the graphical representation below of the two different types of aerosol droplets. Therefore, Saidi does not anticipate each and every element of the claimed invention.



50 micron droplet
submicron drug particle suspended



50 micron droplet
drug in solution

IV. Rejection of the Claims Under 35 U.S.C. § 103

A. Liversidge in view of Moren

Claims 28-40, 42-45, and 47-59 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Liversidge, U.S. Patent No. 5,145,684, in view of Moren, *Aerosols in Medicine, Principles, Diagnosis, and Therapy*, Elsevier Science Publisher, Chap. 13, pp. 321-350 (1993) ("Moren"). Specifically, the claims were rejected because "Liversidge et al. teaches the average particle size, surface modifier, and all other limitations of the presently claimed invention and Moren teaches aerosols and delivery to respiratory tract using poorly soluble drugs such as steroids" and therefore, it would have been obvious to one of skill in the art to prepare the method of delivering an aerosol to lungs by combining the teachings in these two references. Office Action at 6. Applicants respectfully traverse this ground for rejection.

To establish a *prima facie* case of obviousness under 35 U.S.C. § 103(a), the Office must show: (1) at least a suggestion in the prior art of each element recited in the claim at issue, (2) some suggestion or motivation to have combined those elements, as proposed by the examiner, and (3) a reasonable expectation of success, likewise evidenced in the prior art, for the proposed combination. Furthermore, the Office must ascertain that the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made. As described below, the Office has not met this burden.

Moren describes some aqueous systems but teaches that one must choose a form of the drug that is soluble in water. See, Moren at section 4.1.1, page 340. Moren also describes alternative solubilization approaches for drugs that are not water soluble, including the use of cosolvents, solubilizing agents, and inclusion complexes (see Moren at 341). While at the end of section 4.1.1, Moren acknowledges that there may be cases where dissolution is not possible and that a suspension must be used, Moren also teaches that a number of factors need to be considered including investigation of physical stability and redispersion, dose accuracy, and the possible addition of surfactants and thickening agents which may influence the possibility of aerosolizing the liquid. *See* Moren at 341. Given Moren's teaching of various factors that must be considered when attempting to make an aerosol formulation of a poorly water-soluble drug, and that it is highly preferable to utilize water-soluble drugs in aerosol formulations, at the time the claimed invention was made there was no reasonable expectation that attempts to make an aerosol formulation of a poorly water-soluble drug would be successful. Rather, at best Moren is teaching that it may be "obvious to try" to make an aerosol of a poorly water-soluble drug. However, it has long been held that "obvious to try" is not the standard of obviousness under 35 U.S.C. 103. *In re Deuel*, 51 F.3d 1552, 1559, 34 USPQ2d 1210 (Fed. Cir. 1995). Thus, the Office has failed to establish a *prima facie* case of obviousness. Withdrawal of this ground for rejection is respectfully requested.

B. Liversidge in view of Gennaro and Kohler

Claims 28-40, 42-45, and 47-59 were also rejected as allegedly obvious over Liversidge in view of Gennaro, *Remington's Pharmaceutical Sciences,* 17th Ed., Chap. 93, pp. 1670-1677 (1985) ("Gennara"), and Kohler, *Aerosols in Medicine, Principles, Diagnosis, and Therapy*, Elsevier Science Publisher, Chap. 12, pp. 303-319 (1993) ("Kohler"). In particular, the claims were rejected because "Liversidge et al. teaches the average particle size, surface modifier, and all other limitations of the presently claimed invention[,] and Gennaro and Kohler references teach the use of aerosols for poorly soluble drugs and inhalation products and treatment of asthma and other respiratory illness[es]." Office Action at 8. Applicants respectfully traverse this ground for rejection.

Kohler generically describes aerosol formulations but is silent on the issue of inhaled particle size and does not give any indication that one would want to make a nanoparticulate formulation of a drug and aerosolize it. In fact, Kohler teaches away from aqueous aerosols containing drug nanoparticles. The last sentence on page 310 (before Figure 3) states that "the water solubility of the drug and its viscosity determine the amount of drug available in the aerosol droplet after nebulization." This statement implies that the drug must be in solution to be suitable for nebulization as an aqueous aerosol. Accordingly, one of skill in the art would not be motivated to combine Liversidge and Gennaro with the teachings in Kohler to make an aerosol formulation containing a nanoparticulate drug.

Gennaro describes compositions comprising propellants (but not water). There is some discussion of aerosolized suspensions, but in these cases the drug substance is "insoluble in the propellant or propellant/solvent system." Gennaro at 1672. Gennaro's treatment of aqueous aerosols is limited to oil in water emulsions. Gennaro at 1673. Thus, Gennaro does not remedy the deficiencies of the teachings of Liversidge and Kohler to render the claimed invention obvious.

For at least these reasons, the claimed invention is patentable over the combination of cited references and, therefore, withdrawal of this ground for rejection is respectfully requested.

CONCLUSION

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and arguments.

The present application is now in condition for allowance. Early notice to that effect is earnestly solicited.

Examiner Qazi is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date Dec 30, 2005

By _____

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5538
Facsimile: (202) 672-5399

Michele M. Simkin
Attorney for Applicant
Registration No. 34,717

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.